Advisory Committee to the Director

Zika Virus: A Pandemic in Progress

Anthony S. Fauci, M.D.
Director
National Institute of Allergy and Infectious Diseases
National Institutes of Health

June 10, 2016

- Zika background
- Current outbreak in Caribbean and Latin America
- Zika and the USA
- Role of research and development
  - Basic science, epidemiology, natural history
  - Countermeasures: diagnostics, vaccines, therapeutics, vector control

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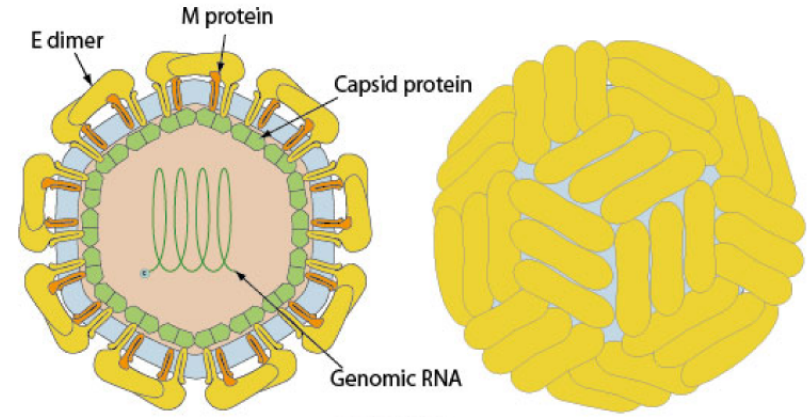
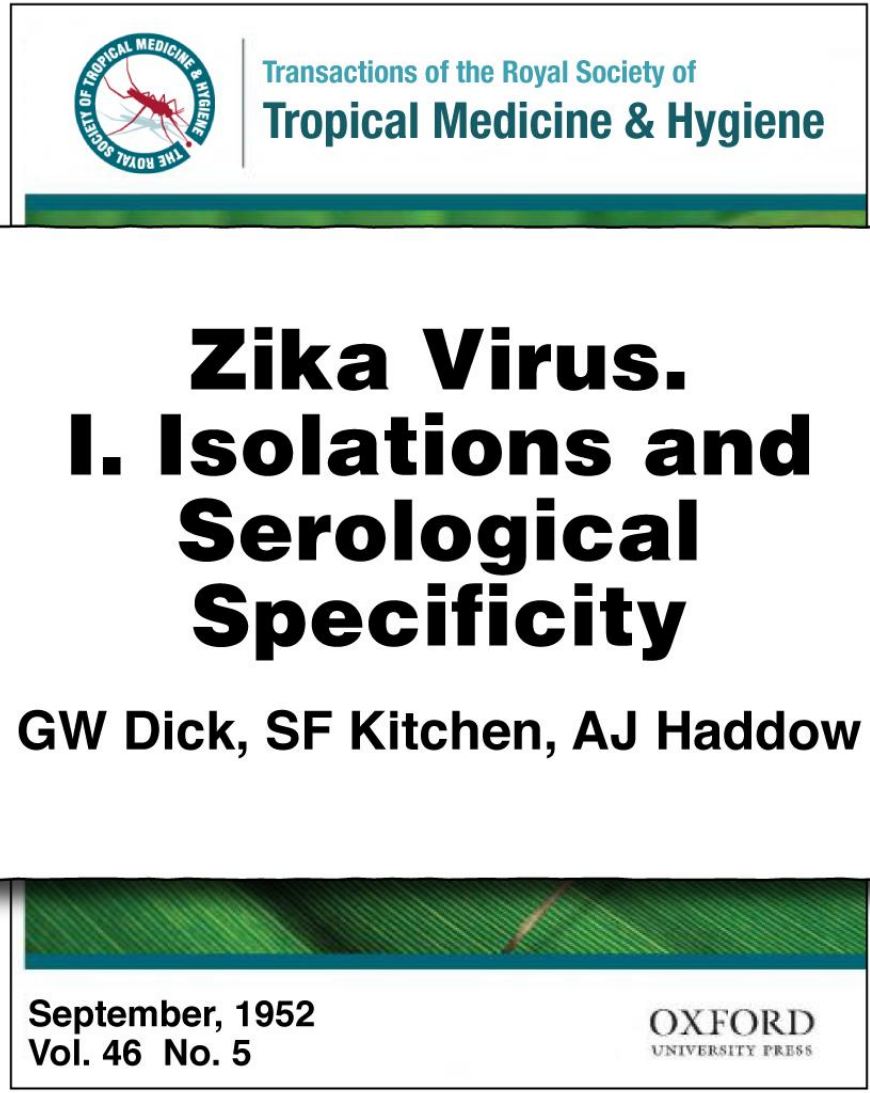
Zika Virus

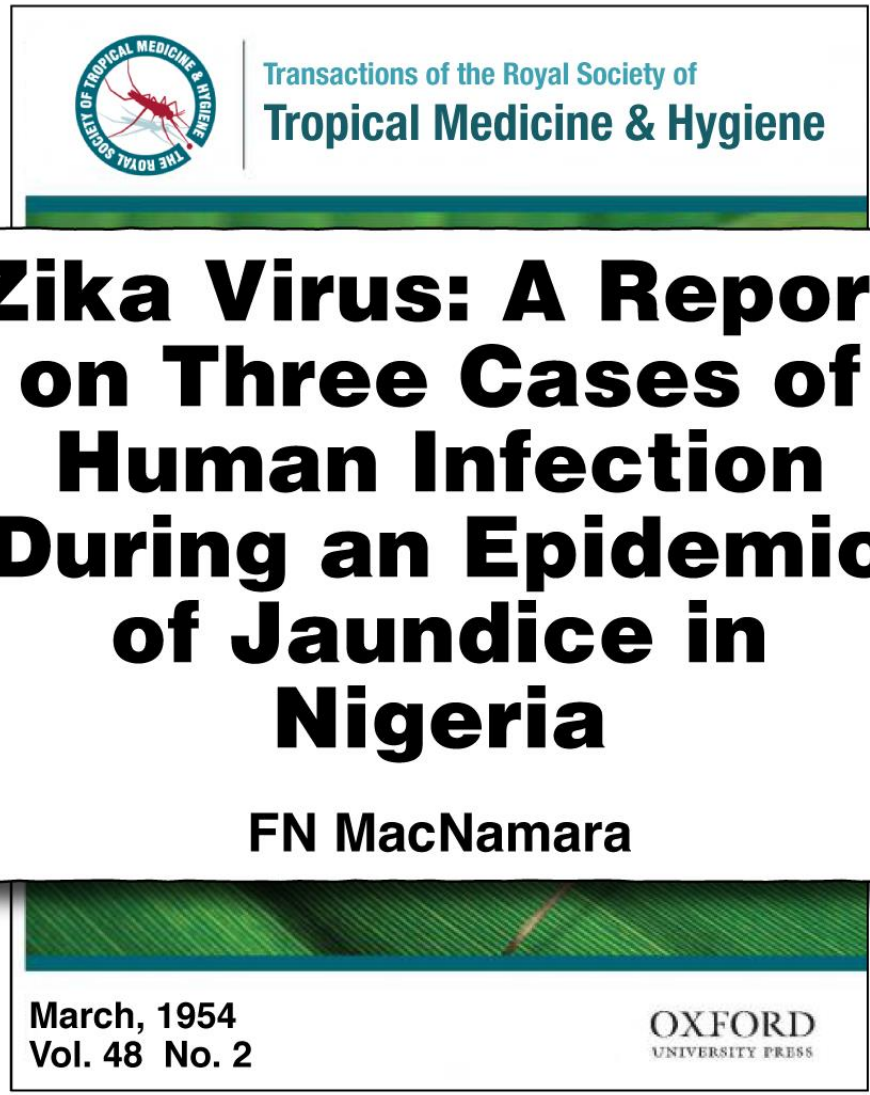
- Single-stranded, enveloped RNA virus
- Family *Flaviviridae*, genus *Flavivirus*
- Closely related to dengue, yellow fever, Japanese encephalitis and West Nile viruses
- Transmitted to humans primarily by *Aedes* mosquito species



Source: CDC



- Virus first isolated from a monkey in the Zika forest of Uganda in 1947



- First human cases reported in Nigeria in 1952

Zika Virus Outbreaks Beyond Africa, 2007-2014

The New England Journal of Medicine
Established in 1812 as THE NEW ENGLAND JOURNAL OF MEDICINE AND SURGERY
VOLUME 360 June 11, 2009 NUMBER 24

Zika Virus Outbreak on Yap Island, Federated States of Micronesia

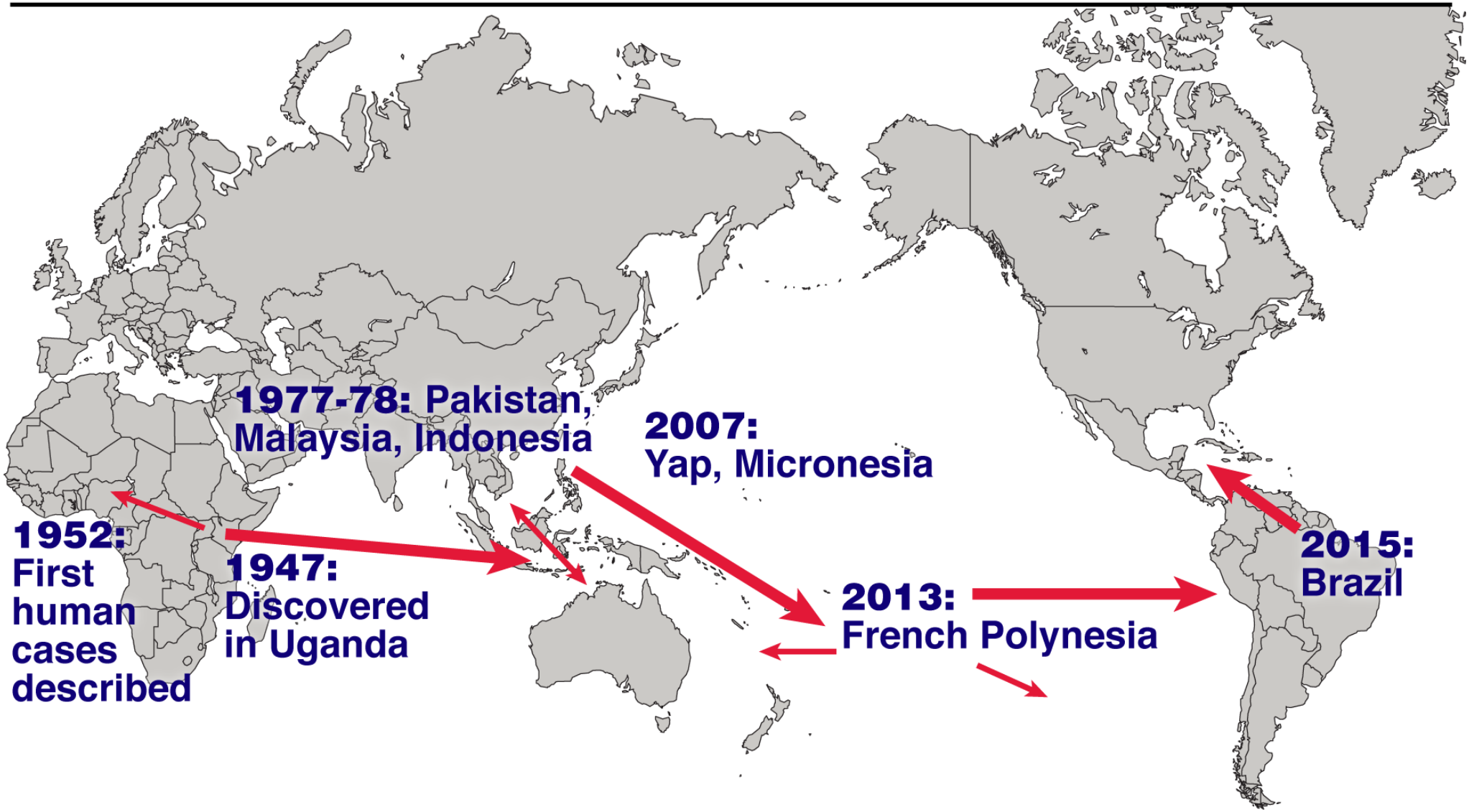
MR Duffy, TH Chen, EB Hayes, et al.

Volume 20 Number 6
June 2014
EMERGING INFECTIOUS DISEASES®

Zika Virus, French Polynesia, South Pacific, 2013

VM Cao-Lormeau, C Roche, D Musso, et al.

Zika Virus Spread, 1947-2016



Source: Lancaster University

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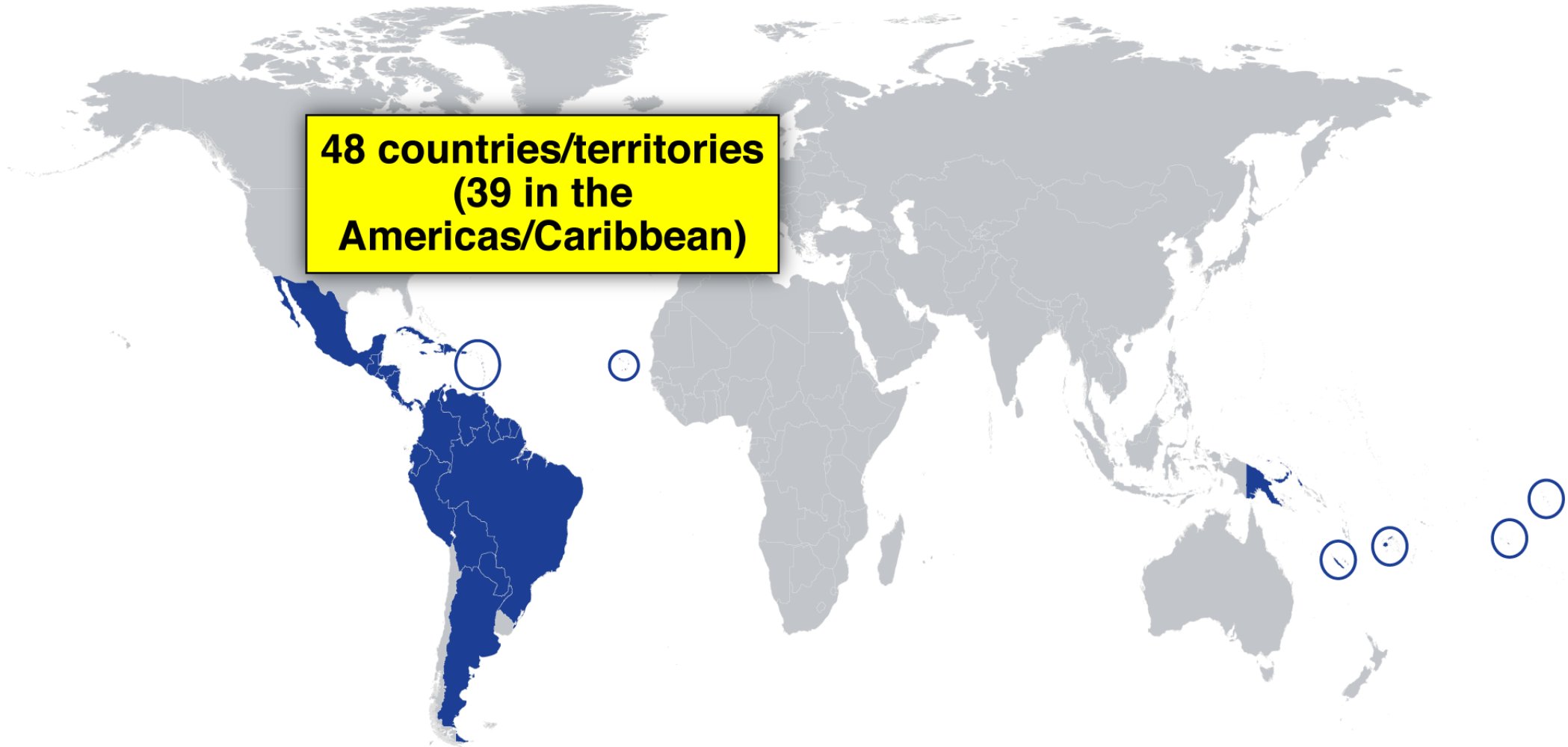
Countries and Territories with Active Zika Virus Transmission – June 2016



Source: CDC, as of May 26, 2016

Microcephaly Attributed to Zika

Normal infant brain and head size

Microcephaly, Colombia 2015

Images: LatinAmericanScience.org

THE LANCET

Published Online February 29, 2016

Guillain-Barré Syndrome Outbreak Associated with Zika Virus Infection in French Polynesia: A Case-Control Study

VM Cao-Lormeau, F Ghawché et al.

- 98% of 42 pts with GBS had anti-Zika virus IgM or IgG, and all (100%) had neutralizing antibodies against Zika virus compared with 56% of 98 pts in control group w/nAbs ($p<0.0001$)
- 88% of 42 patients with GBS reported symptoms of Zika virus infection ~6 days before onset of neurological symptoms
- Based on attack rate for Zika virus of 66% in French Polynesia, risk of GBS in the general population during the outbreak was 24 /100,000 infections

THE LANCET

Published online March 4, 2016

Acute Myelitis Due to Zika Virus Infection

S Mécharles, A Lannuzel, et al.

- 15-year-old girl in Guadeloupe, French West Indies with high concentrations of Zika virus in serum, urine, and cerebrospinal fluid

The New England Journal of Medicine

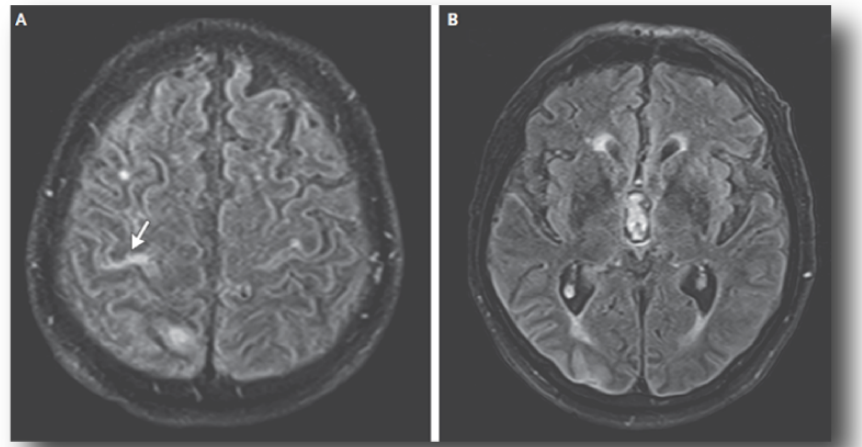
Established in 1812 as THE NEW ENGLAND JOURNAL OF MEDICINE AND SURGERY

Published online March 9, 2016

Zika Virus Associated with Meningoencephalitis

G Carteaux, I Leparc-Goffart et al.

- 81-year-old man in France with meningoencephalitis following cruise in the Pacific (area of New Caledonia, Vanuatu, the Solomon Islands, and New Zealand)
- CSF positive for Zika virus, by PCR and culture



REUTERS

April 10, 2016

Brazilian Scientists Find New Zika-linked Brain Disorder in Adults

- Autoimmune syndrome called acute disseminated encephalomyelitis (ADEM) seen in two patients with Zika virus infection

- Findings presented at the American Academy of Neurology meeting in Vancouver

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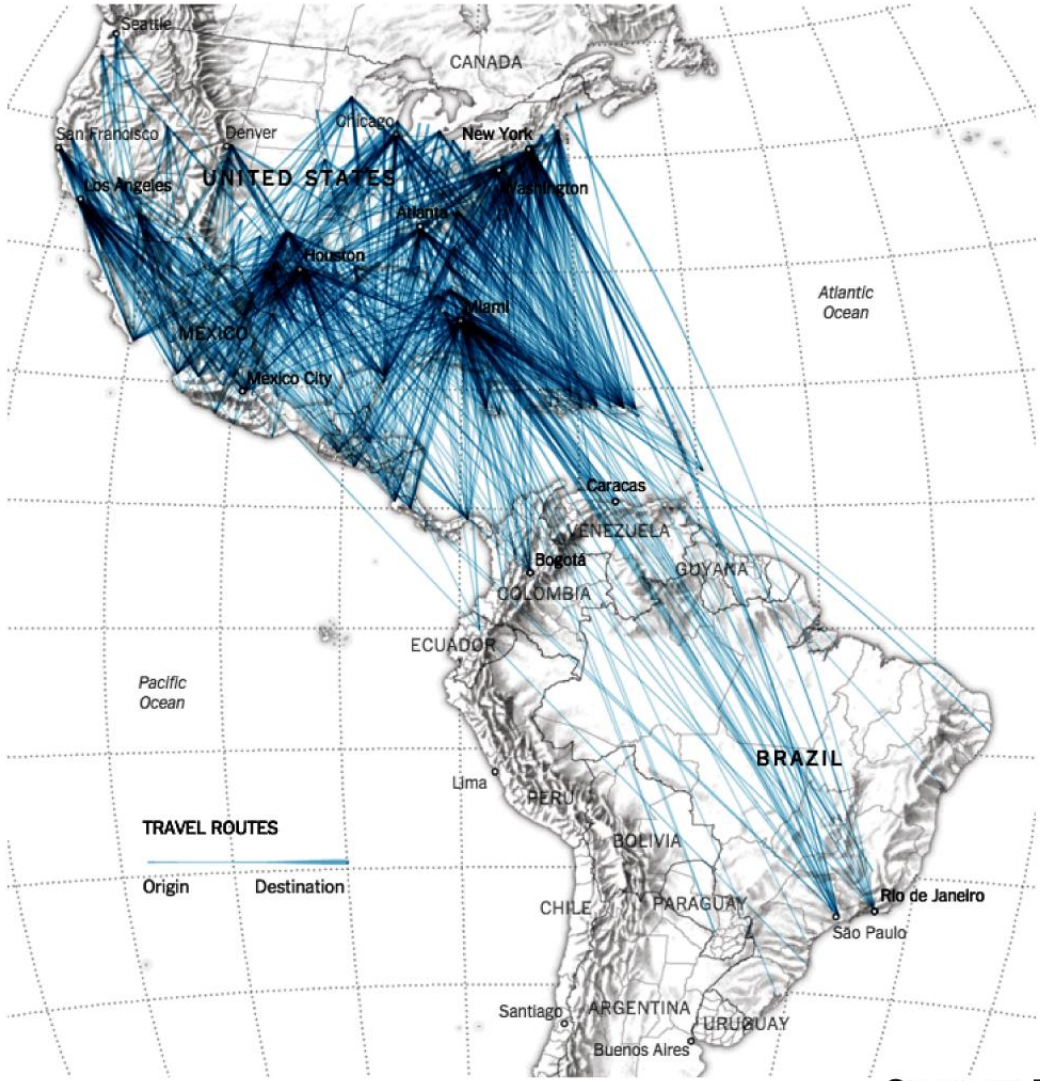
Potential for Imported Cases of Zika in the United States

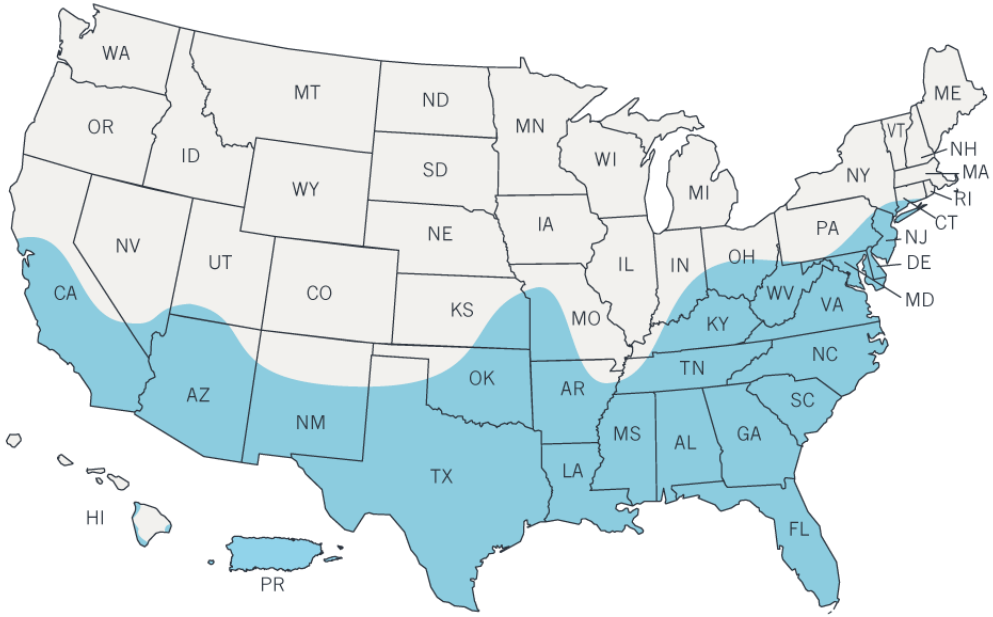


- ~216 million passenger journeys to U.S. annually from areas with local Zika virus transmission
  - 34 M by air
  - 173 M by land
  - 9 M by sea

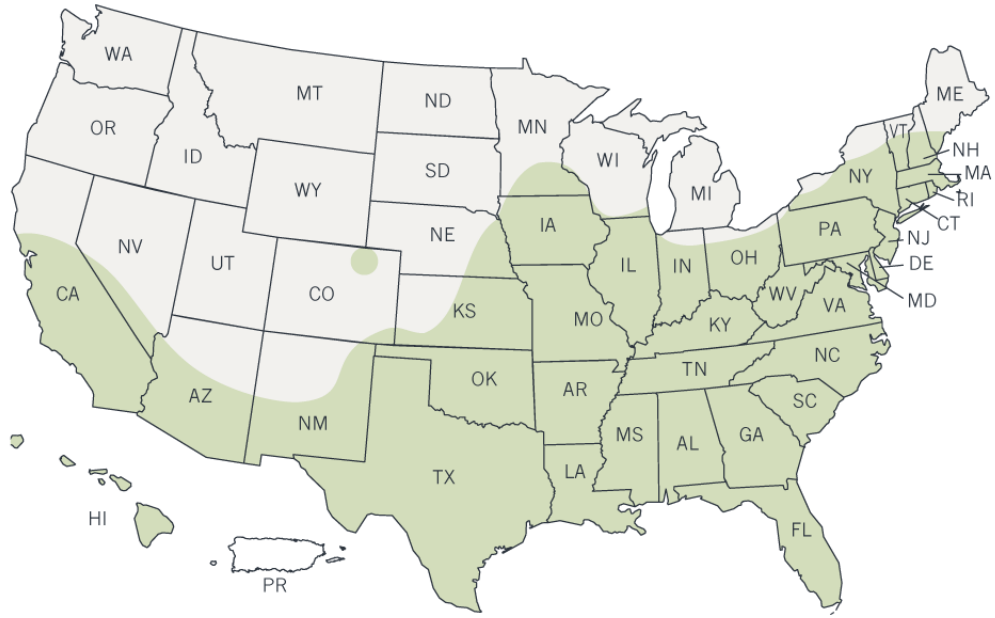
Sources: B Nelson et al. *PLoS Currents Outbreaks*, 5/31/2016; NY Times.

Estimated Range of *Aedes aegypti* and *Aedes albopictus* Mosquitoes in the United States, 2016

Aedes aegypti

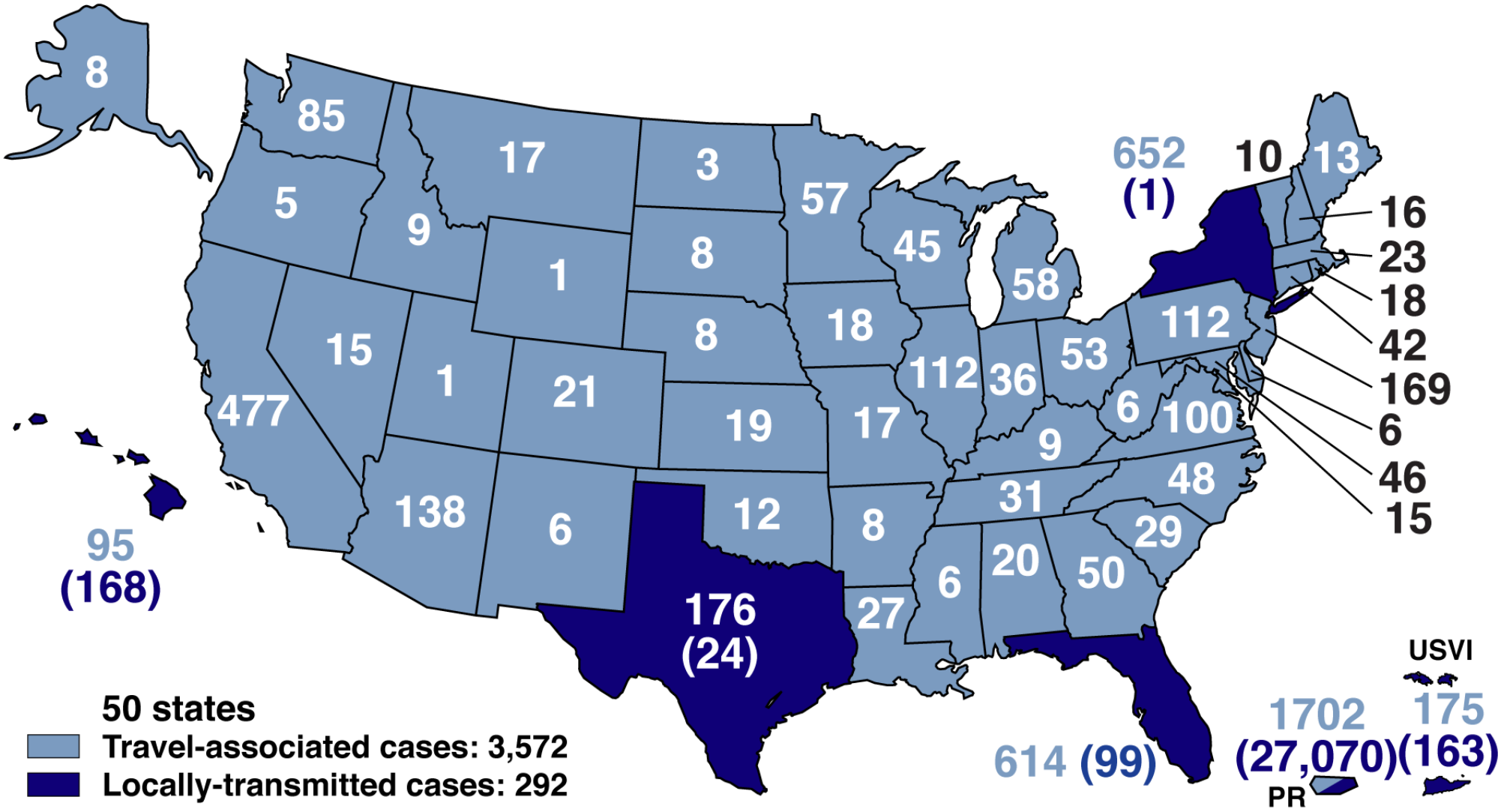


Aedes albopictus



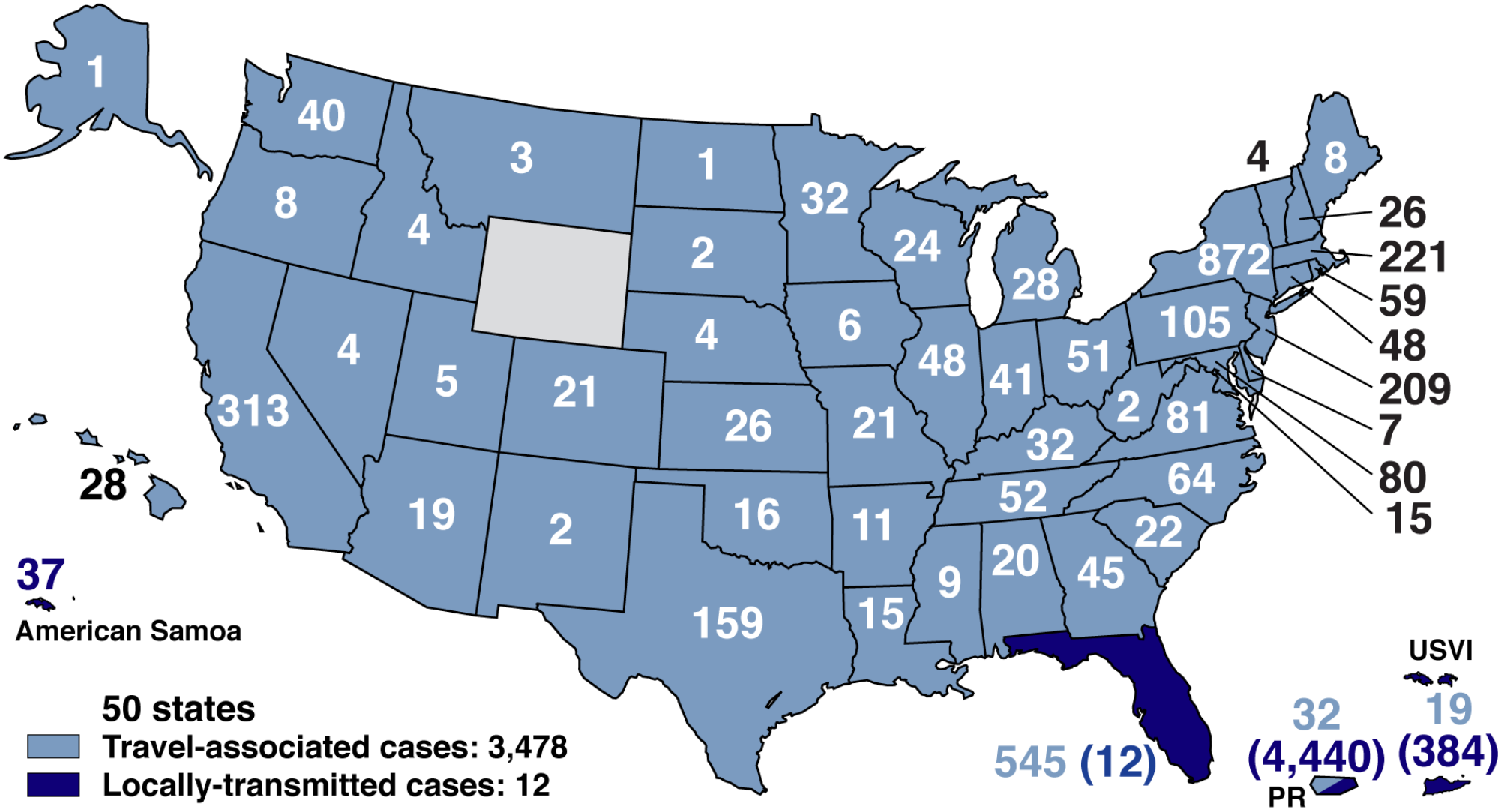
Source: CDC

Dengue Cases in the United States, 2010-2015



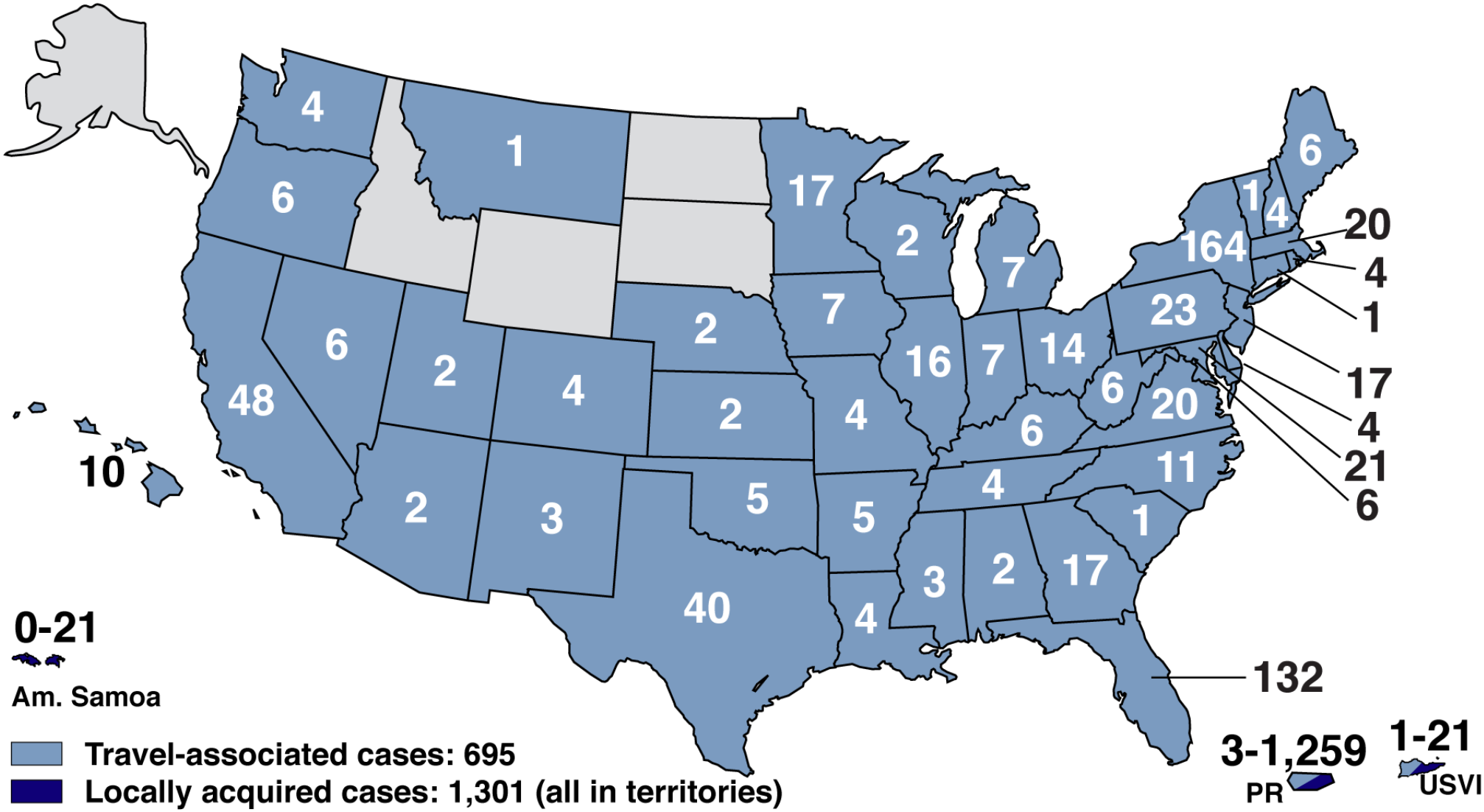
Source: ArboNet. Includes provisional data for 2015.

Chikungunya Cases in the United States, 2014-2015



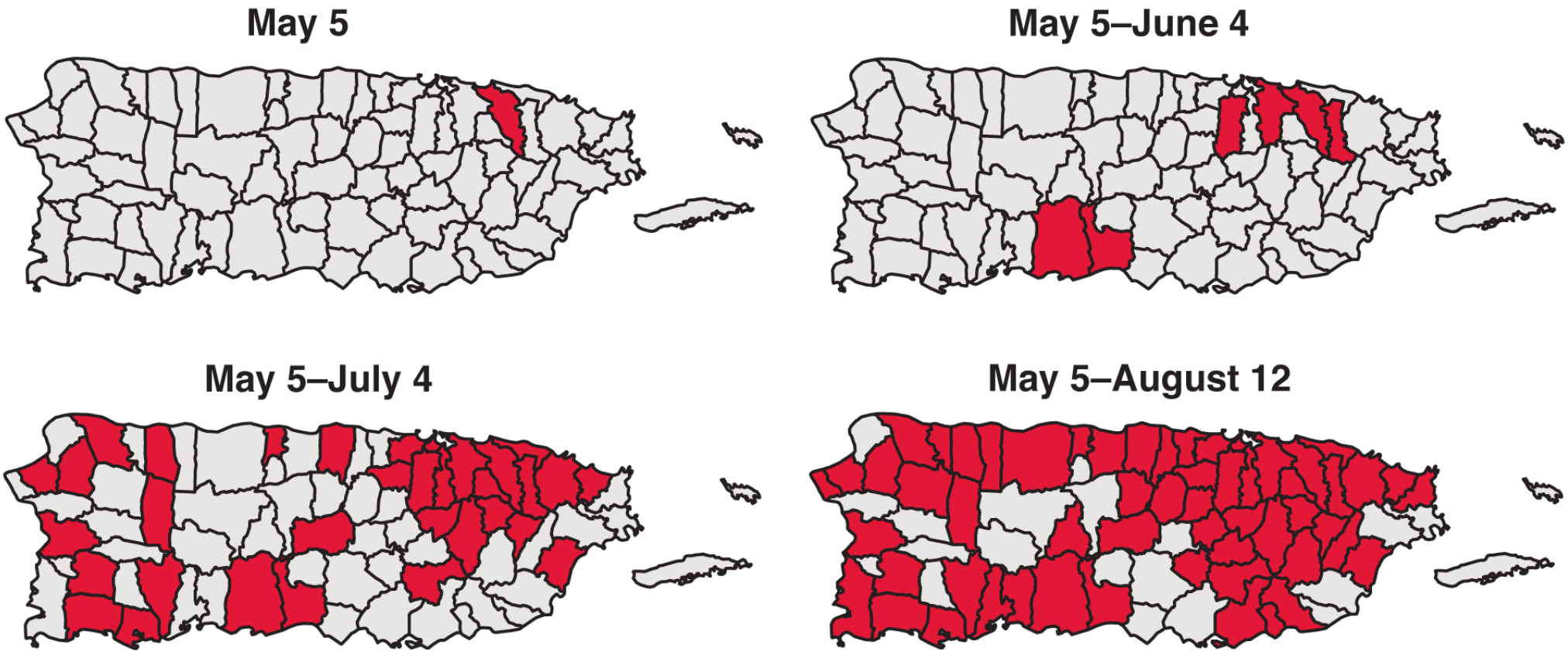
Source: CDC. Cases reported to ArboNET as of 1/12/2016.

Zika Cases in the United States and U.S. Territories, 2015–2016



Source: CDC. Data as of 6/8/16.

Geographic Distribution of Laboratory-Positive Chikungunya Cases — Puerto Rico, May 5-August 12, 2014



Source: *MMWR* 63: 1121, 2014.

Modalities of Transmission of Zika Virus

- Mosquito bites
- Sexual transmission
- Blood transfusion

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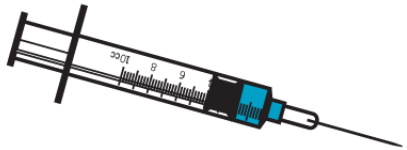
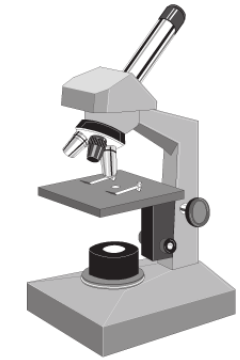
Therapeutics

Novel Vector Control

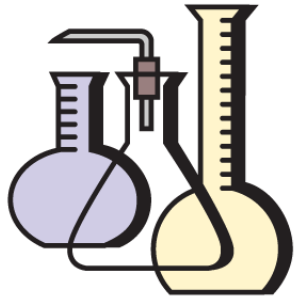


Vaccines

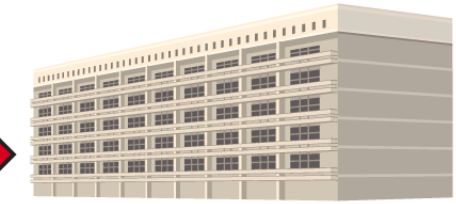
NIAID Countermeasure Research and Development



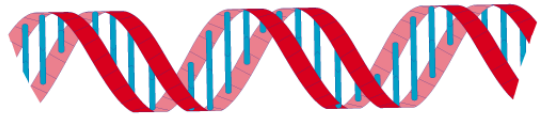
Diagnostics



Basic Research



Expansion of Reseach Capacity



Genomics

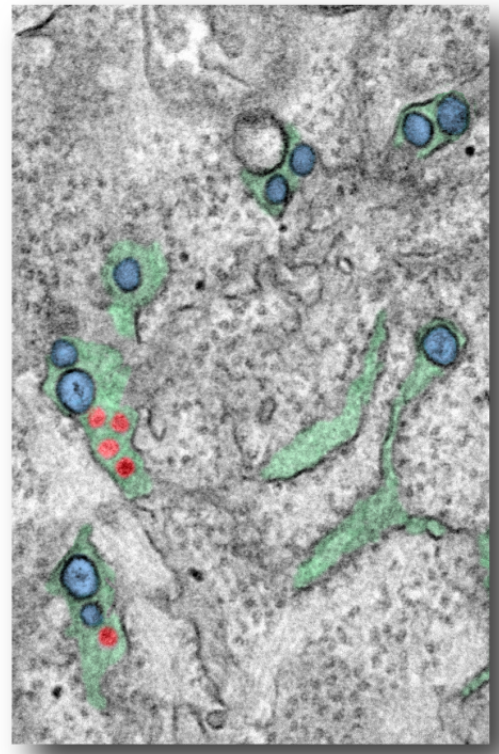
Clinical Research

Zika Virus in the Americas: An HHS Expert Consultation to Accelerate the Development of Countermeasures

March 28-29, 2016, Bethesda, Maryland

Goals

- Review current knowledge
- Identify critical research gaps
- Discuss ways to accelerate research



Credit: RML/NIAID

Supported by NIAID, NICHD, ASPR/BARDA, CDC and FDA

Biomedical Research Response: Basic Science

- Molecular Virology: a) elucidate viral structure; b) compare viruses from different outbreaks
- Pathogenesis of disease
- Studies on immune response (innate and adaptive)
- Establish animal models

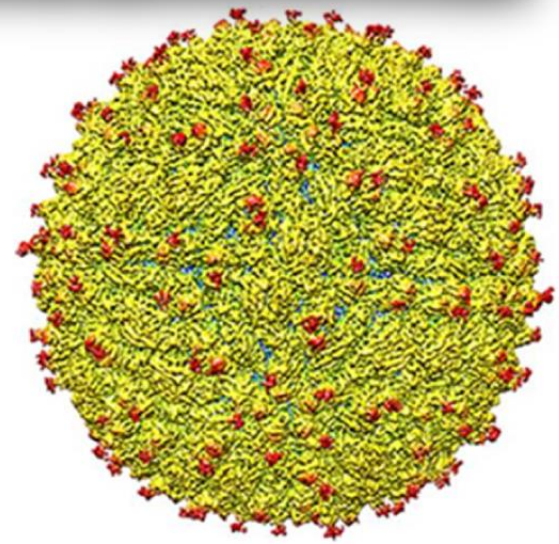
Published online March 31, 2016

Science

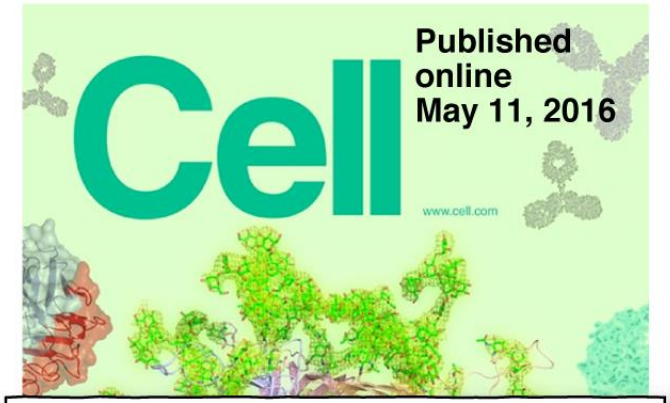
The 3.8 Å Resolution Cryo-EM Structure of Zika Virus

D Sirohi, RJ Kuhn et al.

- Structure largely similar to that of other flaviviruses, except for notable difference in region of E glycoprotein that may be used for attachment to host cells



Zika Virus Causes Microcephaly and Other Fetal Abnormalities in Mice

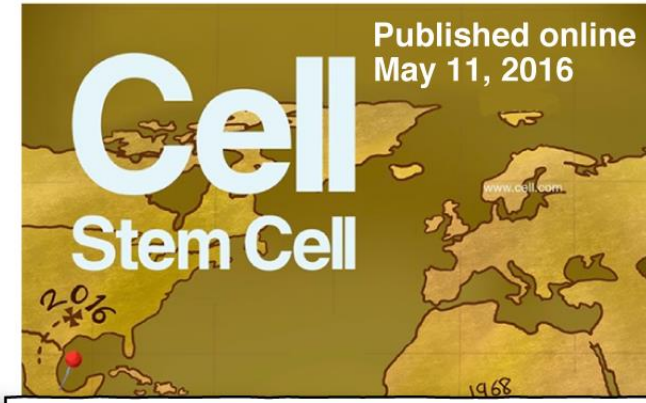


Zika Virus Infection during Pregnancy in Mice Causes Placental Damage and Fetal Demise

JJ Miner, MS Diamond et al.

The Brazilian Zika Virus Strain Causes Birth Defects in Experimental Models

FR Cugola, PC Beltrão-Braga et al.



Zika Virus Disrupts Neural Progenitor Development and Leads to Microcephaly in Mice

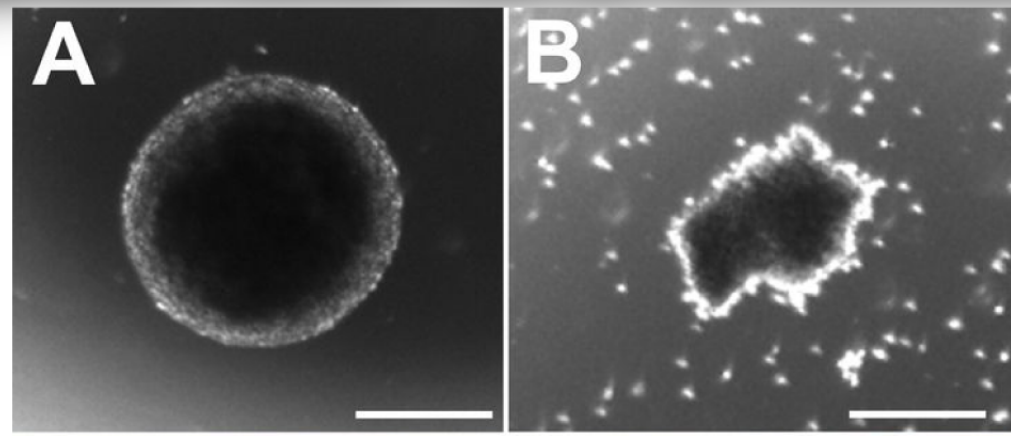
C Li, Z Xu et al.

Published online April 10, 2016

Science

Zika Virus Impairs Growth in Human Neurospheres and Brain Organoids

PP Garcez, SK Rehen et al.



Control

Zika-virus infected neurosphere

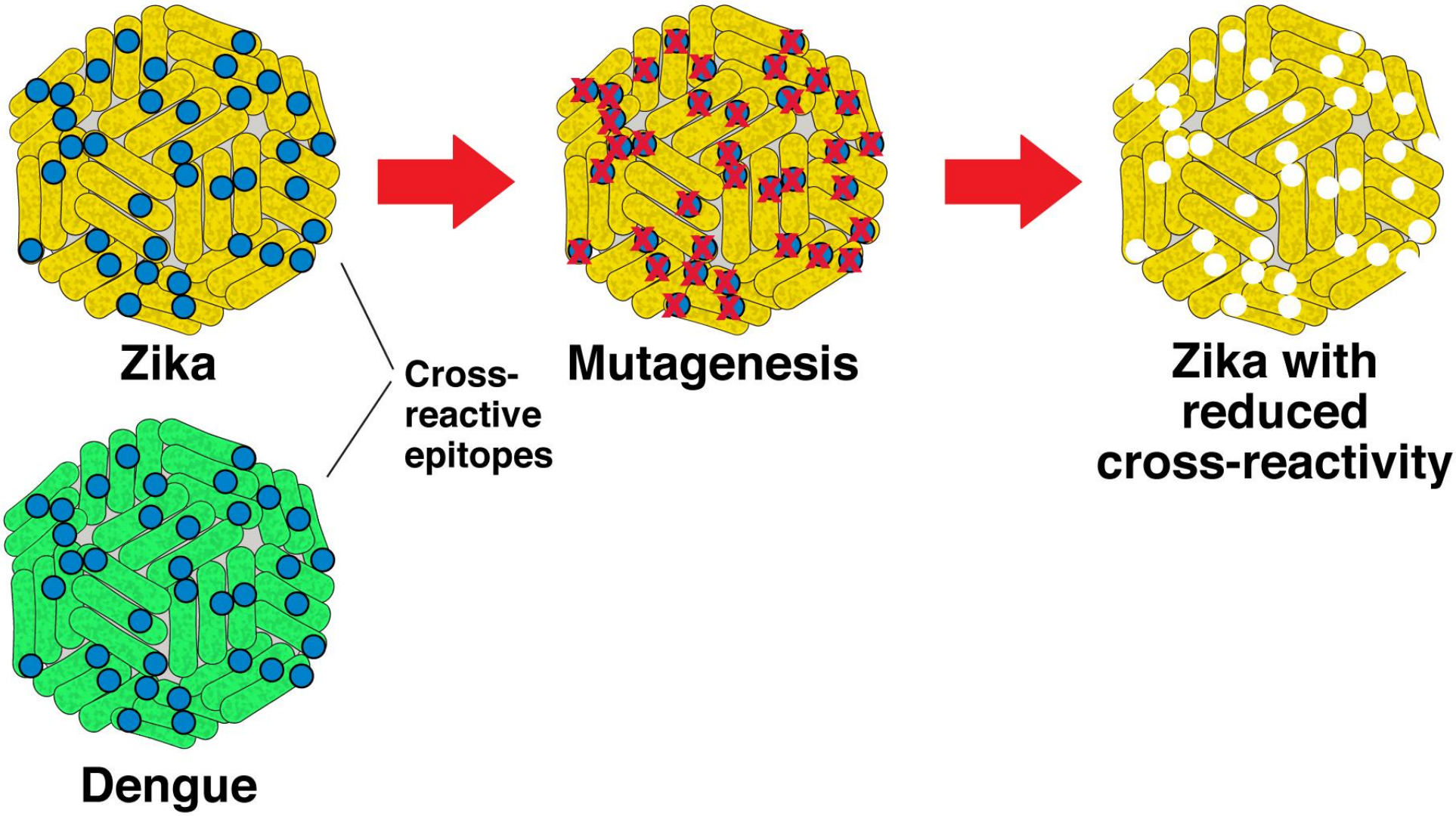
Biomedical Research Response: Epidemiology and Natural History

- Epidemiology and natural history
  - Symptomatic vs. asymptomatic
  - Frequency of sequelae
  - Cohort studies to determine incidence of adverse pregnancy outcomes in Zika-infected pregnant women
- Pathogenesis of microcephaly

Biomedical Research Response: Diagnostics

- **CDC** – Diagnostic and Reference Laboratory in Arbovirus Diseases Branch
- RT-PCR assay for Zika, Dengue and Chikungunya
- Antibody assay for acute infection that will not cross-react with other flaviviruses

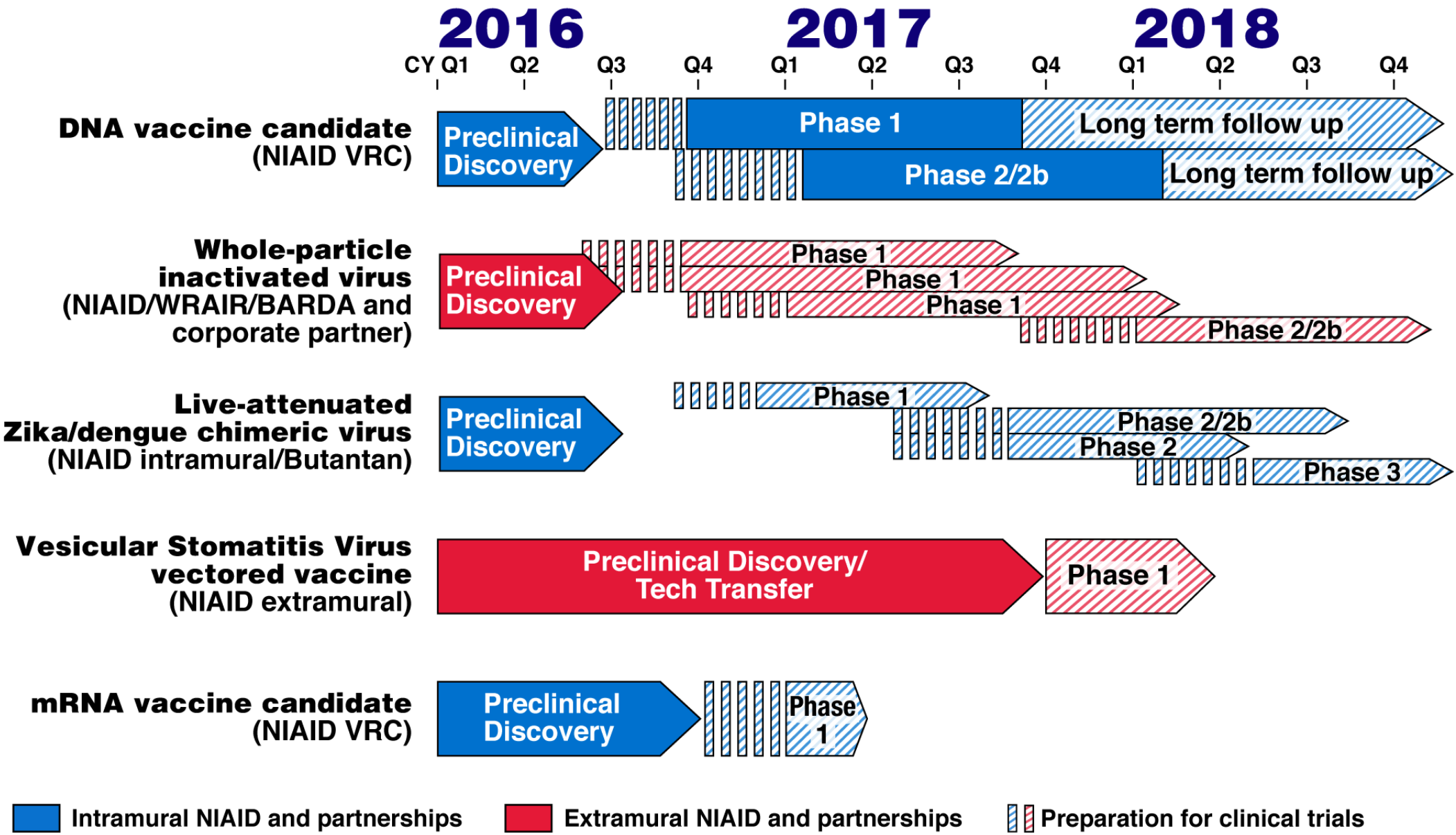
Developing Improved Diagnostics Through Mutagenesis



Biomedical Research Response: Countermeasures – Therapeutics

- Developing *in vitro* antiviral screening assay
- Testing compounds with known activity against other flaviviruses
- Broad screening of compounds without known anti-flavivirus activity

Zika Vaccine Development Timeline

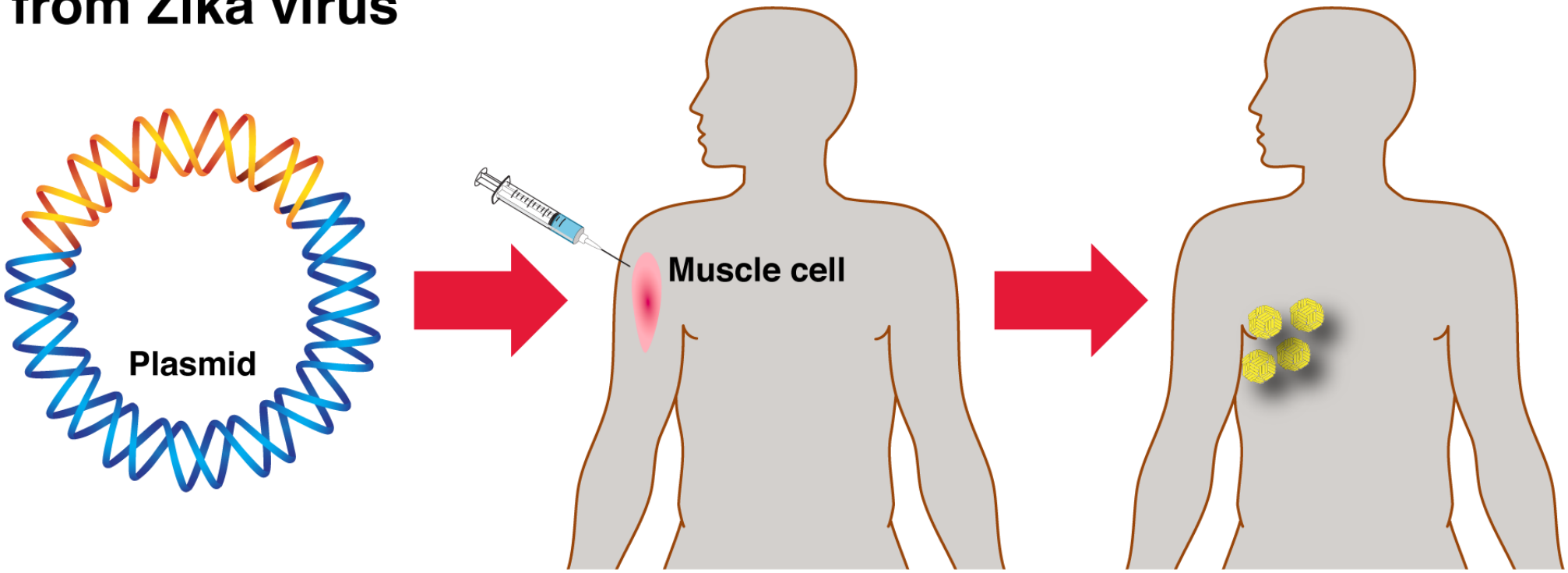


DNA Vaccine Approach

Gene encoding surface protein from Zika virus

Inject DNA containing Zika gene

Body's cells produce virus-like particles, the basis of the vaccine



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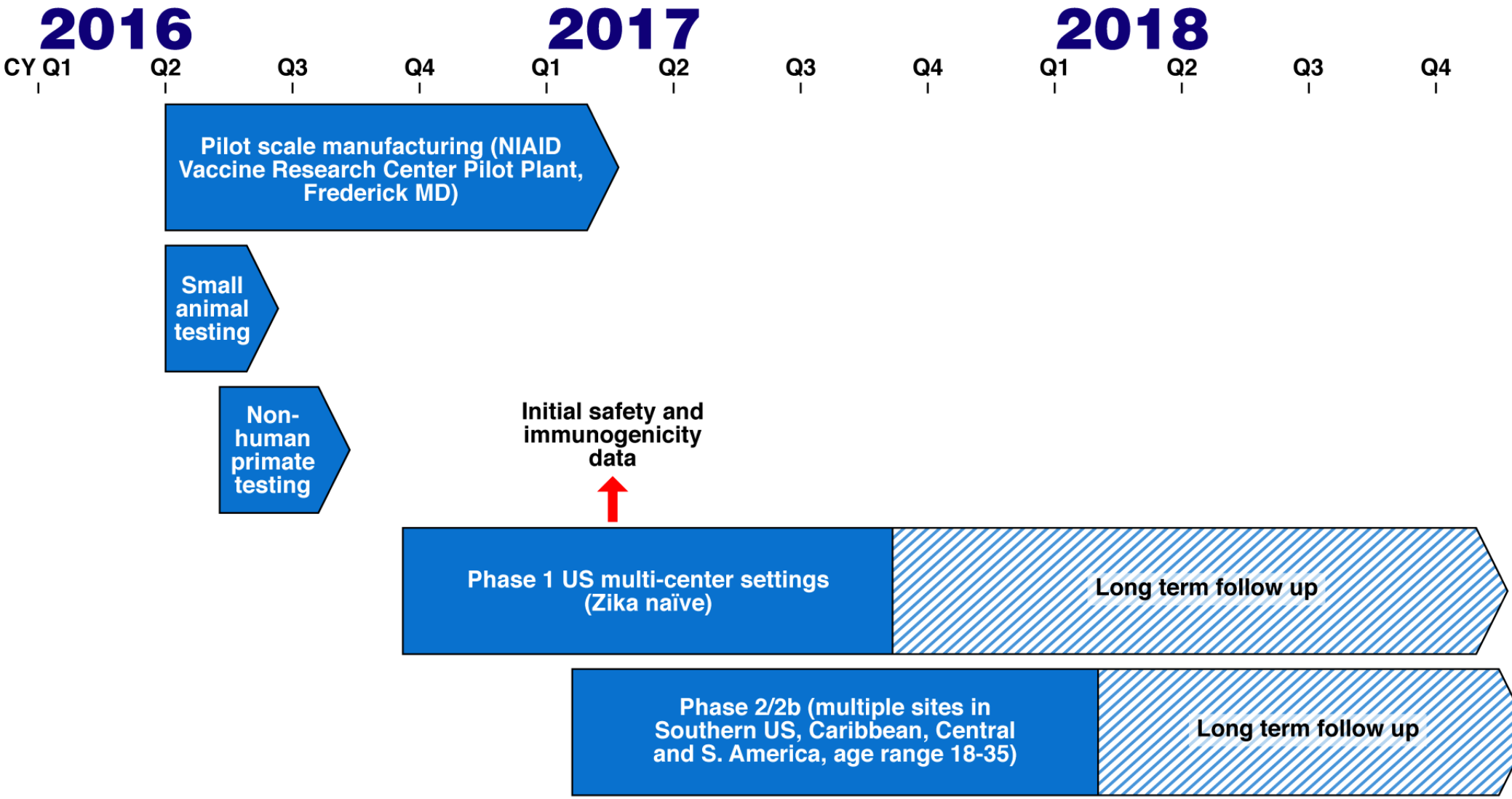


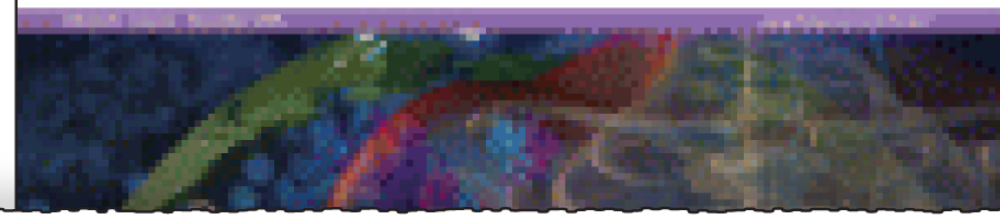
Vaccination for Congenital Infections: Lessons from Rubella

- 1964-65 U.S. rubella epidemic
  - 11,000 miscarriages, 2,100 newborn deaths, 20,000 babies born with congenital rubella syndrome (CRS)
- CRS causes deafness, cataracts, heart defects, often microcephaly
- With MMR vaccine, CRS eliminated in U.S. in 2004

National Library of Medicine

Volume 8, Issue 11 November 2008

THE LANCET Infectious Diseases



Emerging Infections: A Perpetual Challenge

DM Morens, GK Folkers & AS Fauci